all caps

What is claimed is:

CLAIMS

1. A method for transforming a lymphoid cell line to glutamine independence which comprises:

transforming the lymphoid cell line with a vector containing an active glutamine synthetase (GS) gene;

growing the transformed cell line on a medium containing glutamine; and

continuing the growth of the transformed cell line on a medium in which the glutamine is progressively depleted or on a medium lacking glutamine.

2. The method of claim 1, wherein the lymphoid cell line is a myeloma cell line.

3. The method of claim 1 or claim 2, wherein the glutamine-depleted or glutamine-free medium contains asparagine.

4. The method of any one of claims 1 to 3, wherein the lymphoid cell line is transformed with a vector containing both an active GS gene and a gene encoding another selectable marker, such as a gpt gene, or cotransformed with separate vectors encoding GS and the selectable marker respectively.

5. The method of any one of claims 1 to 4, wherein the glutamine in the medium is progressively depleted by dilution with a medium containing aspargine but lacking glutamine.

6. The method of any one of claims 1 to 5, wherein the vector used to transform the lymphoid cell line also contains an active gene coding for a protein heterologous to the lymphoid cell line.

7. The method of any one of claims 1 to 6, wherein the lymphoid cell line is co-transformed with a separate vector containing the active gene coding for the heterologous protein.

8. The method of claim 6 or claim 7, wherein the heterologous protein is an Ig-type molecule.

9. The method of any one of claims 6 to 8, wherein the GS gene comprises a relatively weak promoter and the gene (or genes) encoding the heterologous protein comprises a relatively strong promoter so that in the transformed cell lines, protein synthesis is directed preferentially to the production of the heterologous protein or peptide rather than to the production of GS.

10. A vector for transforming a lymphoid cell line to glutamine independence and to enable it to produce a heterologous protein, the vector comprising a GS gene and a gene encoding the heterologous protein, wherein the vector is arranged such that expression of the GS gene is not hindered by transcriptional interference from the promoter/enhancer transcribing the coding sequence for the heterologous protein to such an extent that glutamine-independent colonies cannot be produced.

11. The vector of claim 10, wherein the GS gene contains a relatively weak promoter, the gene encoding the heterologous protein contains a relatively strong promoter, and the promoter of the GS gene is located upstream of or directs expression in the opposite direction to that of the gene encoding the heterologous protein.

12. The vector of claim 11, wherein the combination for the weak and strong promoters is the SV40 early region and the hCMV-MIE promoters.

13. The vector of claim 10 or claim 11, wherein the vector comprises a GS gene having a weak promoter having downstream therefrom a heavy chain like gene having a strong promoter, there being on the vector a light chain like gene having a strong promoter oriented in the opposite direction to the promoters of the GS and heavy chain like genes.

14. The vector of claim 10 or claim 11, wherein the GS

gene has a weak promoter, the vector contains a light chain like gene and a heavy chain like gene, the heavy and light chain like genes have strong promoters, the three genes are transcribed in the same direction and the GS gene is upstream of the other two genes.

add B1

add C7

add D6